Remarks

Claims 21-40 are pending in the present Application. Of these claims, claims 31-40 have been withdrawn from consideration as a result of an earlier restriction requirement. In the Office Action, the Examiner maintained the earlier restriction requirement. Applicants are now canceling claims 31-40 as non-elected claims, while at the same time preserving the right to file divisional application(s) on the invention of the cancelled claims, if Applicants choose to do so. Thus, claims 21 to 30 are currently under prosecution.

Obviousness-type Double Patenting Rejection

The Examiner has provisionally rejected claim 24 and the scope of claims 21-23, 25-30 wherein R^1 is MR^4 wherein M is phenyl, R^4 is C_{1-6}Alkyl-$NR^{21}SO_2R^{22}$, R^2 is non-heterocyclic, and R^3 is substituted or unsubstituted pyrimidine, under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the pending claims of copending Application No. 10/979,075, in view Tetrahedron, Vol. 42, No. 21, pp. 6039-6045, 1986, authors Rubin et al. (hereinafter "Rubin et al."). The Examiner refers especially to claim 17, 1st and 6th compounds on page 70 of copending Application Serial No. 10/979,075.

The Examiner asserts that the copending claims are drawn to analogous compounds of the instantly "elected" scope of R^4, i.e., $R^4 = C_{1-6}$Alkyl-$NR^{21}SO_2R^{22}$. She also asserts that the difference between the instant elected scope and the copending species is that instead of R^4 being C_{1-6}Alkyl-$NR^{21}SO_2R^{22}$, the copending claims are drawn to compounds wherein an ethylene chain of the C_{1-6}Alkyl linker of the R^4 is replaced by an amide bond. She further asserts that the ethylene linker and an amide bond are considered amide bond surrogate units and refers to Rubin et al., especially page 6039, 9th line from bottom. She further asserts that one having ordinary skill in the art in possession of the copending claims would be motivated to replace the amide bond of the linkage with an amide bond surrogate, i.e., an ethylene chain which would be the instant claims. She asserts that the modification of two sets of compounds with conventional skill in biologically active compounds with amide bond surrogate is prima facie obvious because

one would expect such modification to produce more compounds with analogous activity.

Applicants respectfully disagree with the position taken by the Examiner and traverse this rejection. Applicants respectfully submit that the Examiner has failed to establish a prima facie case of obviousness in the present rejection.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). MPEP 2142.

Here, the Examiner has failed to demonstate any real suggestion or motivation in the cited references to modify the amide linkages of the 1st and 6th compounds on page 70 (claim 17) of the copending application 10/979,075 to ethylene linkage to arrive at the presently claimed invention. Furthermore, she has misapplied Rubin et al. to support her stated motivation, and has resorted to the impermissible use of hindsight in the present obviousness-type double patenting rejection. It is respectfully submitted neither the copending application nor Rubin et al. alone or in combination suggests the presently claimed invention.

Rubin et al. addresses the problem of serious limitations associated with developing peptides as potential therapeutic agents owing to their rapid metabolism and poor transport properties. It suggests overcoming these limitations by creating non-peptide counterparts which would interact similarly with a common receptor inducing identical physiological and pharmacological effects. Rubin et al. discloses that the replacement of the amide bonds in the peptide backbone with amide bond surrogates is an important tool toward the transformation of a peptide toward a non-peptidic peptidomimetic compound,

and lists several isosteric modifications as amide bond surrogates, such as ψ [CH_2-S], ψ [NH-CO], ψ [CH_2-CH_2], ψ [CH_2-NH], ψ [CO-CH_2], ψ [(E) or (Z) CH=CH]. Rubin et al. discloses that one goal of these modifications is to achieve maximal topographical equivalence with the trans-amide bond, and that a close approximation in geometrical terms has been obtained with the ψ [(E) CH=CH] isosteric modification (Rubin et al., page 6039).

The compounds of the present invention however are small molecule CCR5 antagonists and are not peptides. Rubin et al. deals exclusively with peptides and the desirability of converting peptides into non-peptidic counterparts for the reasons set forth in the previous paragraph. Thus the teaching of Rubin et al. provides no motivation for transforming the presently claimed compounds which are not peptides. Furthermore the claims of the copending application 10/979,075 also provide no motivation to transform the amide bond to an alkylene linkage. Therefore the Examiner's assertion that the motivation to transform the amide bonds in the compounds covered by the claims of the copending application 10/979,075 with an amide bond surroagate, such as an ethylene chain is to produce more compounds with analogous activity, therefore, finds no basis either in the teaching of the claims of the copending application or in Rubin et al., alone or in combination. The Examiner must have resorted to the impermissible use of hindsight in the present rejection.

Even assuming *arguendo*, that Rubin et al proposes such a transformation even for non-peptide small molecules, which is not admitted herein, the transmoration of an amide to an ethylene linkage is one of six or seven possibilities (the others being conversion to CH_2-S, NH-CO, CH_2-NH, CO-CH_2, and (E) or (Z) CH=CH), and Rubin et al. provides no motivation to pick and choose the transformation to ethylene linkage over others. This is so especially in view of the teaching in Rubin et al. that one goal of these modifications is to achieve maximal topographical equivalence with the trans-amide bond, and that a close approximation in geometrical terms has been obtained with the ψ [(E) CH=CH] isosteric modification (Rubin et al., page 6039).

It is respectfully submitted that the Examiner has failed to establish a case of prima facie obviousness and she is respectfully requested to withdraw the present rejection.

CONCLUSION

Applicants respectfully request prompt reconsideration of elected subject matter of claims 21-30, and an early allowance of the application.

If the Examiner wishes to comment or discuss any aspect of this application or response, applicants' undersigned attorney invites the Examiner to call him at the telephone number provided below.

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